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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,195	11/14/2003	Joffre B. Baker	GHDX-005	5745

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EXAMINER	
SHAW, AMANDA MARIE	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
03/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/714,195	BAKER ET AL.	
	Examiner	Art Unit	
	AMANDA SHAW	1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 February 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: See *Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *none*.
   Claim(s) objected to: *60*.
   Claim(s) rejected: *31,35-38,41-47,51,52,59,60 and 62*.
   Claim(s) withdrawn from consideration: *40 and 64*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____

13. ☐ Other: _____.

/Carla Myers/
Primary Examiner, Art Unit 1634

Continuation of 3. NOTE: The proposed amendment to claim 31 raises new issues because the scope of the claims has changed. Previously the claims recited a "wherein" clause stating that "the normalized level of LAMC2 RNA transcript correlates with clinically beneficial patient response to treatment with an ErbB1 inhibitor. However the "wherein" clause has been amended to recite "an increased normalized level of LAMC2 RNA transcript correlates with resistance of the colon cancer to treatment with an ErbB1 inhibitor." Particularly the amendment raises new issues necessitating further search and consideration because the claims did not previously state that "increased" levels of LAMC2 correlate with "resistance of the colon cancer". As a result the proposed amendments do not place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

Continuation of 11. does NOT place the application in condition for allowance because: With regard to the objections, the Applicants arguments pertain both to the pending claims and the claims as amended. The Applicants argue that claim 60 recites a reasonable number of sequences for examination purposes (i.e. 10 sequences). Therefore this objection should be withdrawn. This argument has been fully considered but is not persuasive because claims to polynucleotide sequences are considered for independence, relatedness, distinction and burden as for claims to any other type of molecule. In the instant application each gene constitutes an independent and distinct invention within the meaning of 35 USC 121 since each gene consists of a different nucleotide sequence, has a different melting point, a different specificity of hybridization and encodes for a protein having a different biological activity. Therefore, with regard to claim 60 a search for multiple genes or multiple combinations of genes in addition to LAMC2 is an undue burden on the office. Therefore until claim 31 is found allowable, claim 60 will be objected to for reciting non elected RNA transcripts. Additionally it is noted for the record that if claim 31 is found allowable it does not necessarily mean that claim 60 will be allowable because the examiner will first have to consider if the specification provides enablement for each of the additional genes recited by claim 60.

Regarding the enablement rejection the Applicants arguments pertain to both the pending claims and the claims as amended. Although the arguments that pertain solely to the claims as amended are moot in view of the non entry of the after final amendment it is noted that even if these claims had been entered the claims would still be problematic because they do not recite how one would use the LAMC2 level to make the prediction. While the amended claims state that "an increased normalized level of LAMC2 RNA transcript correlates with resistance of the colon cancer" it is not clear if the correlation is a positive or negative correlation.

The Applicants then argue that the papers by Evans and Lee cited in the previous office action are irrelevant to the instant claims. This argument has been fully considered but is not persuasive because these are both general citations that describe the state of the art and the unpredictability of correlating gene expression levels with an individuals response to treatment.

The Applicants next argument is that since they have shown a negative correlation between LAMC2 levels and patient response to at least 3 classes of ErbB1 inhibitors they believe the claims are enabled for ErbB1 inhibitors in these classes, and specifically erlotinib, cetuximab, or gefitinib. This argument has been fully considered but is not persuasive. As stated in the previous office action the declaration and specification as originally filed do not provide data which separately establish the levels of LAMC2 mRNA in subjects showing a beneficial response to erlotinib, subjects showing a beneficial response to cetuximab and subjects showing a beneficial response to gefitinib. In the absence of a clear showing of an association between increased LAMC2 mRNA levels and a clinically beneficial response to each of the drugs erlotinib, cetuximab, or gefitinib, it remains unpredictable as to whether LAMC2 mRNA levels can be used to predict the likelihood of a beneficial response to these drugs..